Quantification of modulated blood oxygenation levels in single cerebral veins by investigating their MR signal decay ☆

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Abstract

The transverse magnetization of a single vein and its surrounding tissue is subject to spin dephasing caused by the local magnetic field inhomogeneity which is induced by the very same vessel. This phenomenon can be approximated and simulated by applying the model of an infinitely long and homogeneously magnetized cylinder embedded in a homogeneous tissue background. It is then possible to estimate the oxygenation level of the venous blood by fitting the simulated magnetization-time-course to the measured signal decay. In this work we demonstrate the ability of this approach to quantify the blood oxygenation level (Y) of small cerebral veins in vivo, not only under normal physiologic conditions ($Y_{native} = 0.5–0.55$) but also during induced changes of physiologic conditions which affect the cerebral venous blood oxygenation level. Changes of blood's oxygenation level induced by carbogen (5% CO_2, 95% O_2) and caffeine were observed and quantified, resulting in values of $Y_{carbogen} = 0.7$ and $Y_{caffeine} = 0.42$, respectively. The proposed technique may ultimately help to better understand local changes in cerebral physiology during neuronal activation by quantifying blood oxygenation in veins draining active brain areas. It may also be beneficial in clinical applications where it may improve diagnosis of cerebral pathologies as well as monitoring of responses to therapy.

Quantifizierung modulierter Blutsauerstoffgrade in einzelnen zerebralen Venen anhand ihres MR-Signalzerfalls

Zusammenfassung

Die transversale Magnetisierung eines venösen Gefäßes und dessen Umgebung unterliegt der Spindephasierung, die durch die vom selben Gefäß erzeugten, lokalen Magnetfeldinhomogenitäten verursacht wird. Dieses Phänomen kann unter Zuhilfenahme des Modells eines unendlich langen, homogen magnetisierten Zylinders, der in einer homogenen Umgebung eingebettet ist, approximiert und simuliert werden. Durch Anpassen des simulierten Verlaufes an die Messdaten ist es möglich, auf den Blutoxygenierungsgrad (Y) in der Vene zu schließen. In der vorliegenden Arbeit wurde dieser Ansatz erfolgreich angewendet und die Blutoxygenierung kleiner, zerebraler Venen in vivo bestimmt. Unter normalen physiologischen Bedingungen wurde $Y_{nativ} = 0,5–0,55$ ermittelt. Änderungen der venösen Blutoxygenierung, die durch Atmung von Karbogen (5%CO_2, 95%O_2) bzw. Koffeineinnahme induziert wurden, konnten detektiert und quantifiziert werden ($Y_{Karbogen} = 0,7$, $Y_{Koffein} = 0,42$). Basierend auf diesen Ergebnissen könnte die hier vorgestellte Methode zu einem besseren Verständnis lokaler Änderungen zerebraler physiologischer Parameter bei neuronaler

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Aktivierung beitragen. Auch bei klinischen Anwendungen könnte die Methode hilfreich sein, zerebrale Läsionen genauer zu charakterisieren und den Verlauf einer Therapie zu überwachen.

Keywords: MRI, SWI, BOLD, blood oxygenation, carbogen, caffeine

Schlüsselwörter: MRT, SWI, BOLD, Blutoxygenierung, Karbogen, Koffein

Introduction

The detection and potential quantification of oxygenation in blood or tissue is of great importance for understanding normal physiology as well as for understanding progression and treatment in a variety of diseases. Venous hemoglobin saturation with oxygen (Y) is an important physiological parameter for assessment of tissue oxygenation. For instance, monitoring oxygen saturation of venous blood allows estimation of the balance of global oxygen delivery and cerebral oxygen consumption. Usually, measurements of jugular venous oxygen saturation are performed by insertion of a catheter into the internal jugular vein bulb to obtain blood samples that are then analyzed. This procedure, however, is invasive, prone to complications and allows only the extraction of global oxygenation saturation because of the large draining vein [1]. Alternative methods to measure oxygen *in vivo*, such as the use of pO_2 microelectrodes [2,3], near infrared spectroscopy (NIRS) [4,5] or ^{15}O-PET [6,7] are also either invasive, have low spatial resolution and poor quantification or are expensive and not ubiquitously available. With microelectrodes there is always the limitation of acute tissue damage. Furthermore, the fact that the probe consumes oxygen during measurements and may be slow in its response may actually influence the results. NIRS allows measuring changes of oxyhemoglobin and deoxyhemoglobin concentration in cerebral vessels by means of the characteristic absorption spectra of hemoglobin in the near infrared range. Although an elegant non-invasive optical method it suffers from limited penetration of the light into the tissue and the difficulty to measure absolute cerebral oxygen saturation, because this requires measurement of the path length of the absorbed infrared light.

In contrast, magnetic resonance imaging (MRI) is a versatile noninvasive modality with high spatial resolution and superb soft tissue contrast that is able to extract a variety of physiological parameters including blood oxygenation extraction fraction (OEF) maps of the human brain. OEF is an important indicator of brain tissue viability, and the possibility to obtain estimates of this parameter has been already demonstrated successfully by several investigators [8–11].

Recently, we reported on a method that is capable of quantifying non-invasively the cerebral blood oxygenation level in small, single venous vessels *in vivo* by using MRI [12]. The approach we used is to measure and to simulate the signal decay of a single voxel which is traversed by single venous vessel as a function of time. This signal decay is not only governed by irreversible spin-spin interactions (T_2-decay) but also by the additional spin dephasing associated with the static field inhomogeneity pertaining to the vein (T_2'-decay). Since the local field distribution inside and outside a vein depends on the vein's blood oxygenation level, Y, vessel diameter and orientation with respect to the main magnetic field, it is possible to estimate these parameters by analyzing the signal-time course. In fact, non-mono exponential and even oscillating signal decays *in vivo* were first reported by Barth et al. who assessed neuronal activations at multiple echo times at 1.5 T [13,14] and later 3 T [15]. The authors correctly ascribed this signal modulation to the presence of single veins within the voxels or to larger veins nearby the voxels.

Furthermore, since induced changes of the venous blood oxygenation saturation affect the blood oxygenation level dependent (BOLD) signal [16] of veins and thus contrast in susceptibility weighted imaging (SWI) [17–20] which utilizes the BOLD-mechanism, it should then be possible to monitor these changes of the venous blood oxygenation level Y. Contrast modulation of the venous system has been demonstrated on SWI images by application of carbogen ($5\%CO_2$, $95\%O_2$) [21] and caffeine [22]. Inhalation of carbogen increases cerebral blood flow (CBF) and blood volume, thus increasing oxyhemoglobin (oxy-Hb) content in venous blood, whereas caffeine is known to have a vasoconstrictive effect on cerebral vessels. Although induced relative signal changes of veins were determined in the work referred to above [21,22], the extraction of quantitative data of the blood oxygenation level in a single cerebral venous vessel and its changes was limited in these studies.

The aim of the presented work was to apply the previously proposed method [12] *in vivo* and to quantify venous blood oxygenation levels in single veins under different physiological conditions induced by breathing carbogen or ingestion of caffeine.